Original Research
JCAM

ANALYSIS OF MATERNAL AND NEONATAL OUTCOMES IN DIFFERENT TYPES OF PLACENTA PREVIA AND IN PREVIA-ACCRETA COEXISTENCE

PLASENTA PREVİANIN FARKLI TİPLERİNDE VE PREVİA-AKRETA BİRLİKTELİĞİNDE MATERNAL VE NEONATAL SONUÇLARIN ANALİZİ

MATERNAL-NEONATAL OUTCOMES IN PLACENTA PREVIA

Alev Özer, Hilal Sakallı, Bülent Köstü, Şakir Aydoğdu
Department of Obstetrics and Gynecology, Kahramanmaraş Sütçü İmam University Hospital, Kahramanmaras, Turkey

Bu makale, 5-9 Ekim 2016 Antalya'da düzenlenen 14. Ulusal Jinekoloji ve Obstetri Kongresinde Poster olarak sunulmuştur.

Öz
Amaç: Plasenta previanın (PP) farklı tipleri ile previa-akretada maternal ve neoanatal sonuçların karşılaştırılması amaçlanmıştır. Gereç ve Yöntem: Bu retrospektif vaka-kontrol çalışmasına 3. basamak bir referans hastanesinde Ocak 2014-Aralık 2015 tarihleri arasında antenatal ultrasonografi incelemesi ile PP tanısı almış 213 tekil gebe dahil edildi. Hastalar 5 grupta kategorize edildi: 1-aşağı yerleşimli, 2-marginal, 3-parsiyel, 4-komplet PP ve 5-PP ve plasenta akretanın (previa-akreta) bir arada olduğu olgular. Bulgular: Previa-akreta grubunda ortalama gravida, parite ve sezaryenle doğum (SD) sayısı anlamlı olarak yüksek saptandı. Diğer gruplarla karşılaştırıldığında previa-akreta grubunda daha düşük postoperative hemoglobin seviyesi ve daha uzun hastande yatış süresi saptandı. Ortalama kan kaybı, yoğun bakım ünitesine (YBİ) yatış ve histerektomi oranı komplet previa ve previa-akreta grubunda anlamlı olarak yüksekti. Preterm doğum oranı previa-akreta grubunda diğer gruplardan anlamlı olarak daha yüksek saptandı. Doğumdaki ortalama gebelik haftası ve doğum ağırlığı açısından gruplar benzerdi. Komplet olan ve komplet olmayan (aşağı-yerleşimli, marginal ve parsiyel) PP olgularının karşılaştırılmasında, komplet previa grubunda kan ürünü transfüzyonu ihtiyacı, plasenta akreta, peripartum histerektomi, postpartum kanama ve YBÜ'de takip riski artmıştı. Tartışma: Plasenta previa ve akretanın birlikteliği maternal-neonatal morbiditeyi arttırmaktadır. Komplet PP olgularıyla karşılaştırıldığında, aşağı yerleşimli, marjinal ve parsiyel PP maternal-neonatal morbiditeyi artırmamaktadır.

Anahtar Kelimeler
Plasenta Previa; Plasenta Akreta; Maternal Sonuçlar; Neonatal Sonuçlar

Abstract
Aim: It was aimed to compare the maternal and neonatal outcomes between different types of placenta previa (PP) and previa-accreta. Material and Method: This retrospective case-control study included 213 singleton pregnancies diagnosed with PP using the antenatal ultrasonographic examination in a tertiary reference hospital between January 2014 and December 2015. The patients were categorized into 5 groups: 1-low-lying, 2-marginal, 3-partial, 4-complete, and 5-coexistence of PP and placenta accreta (previa-accreta). Results: Mean gravida, parity, and number of previous caesarean sections (CS) were significantly higher in the previa-accreta group. Compared to other groups, significantly lower postoperative haemoglobine level and longer hospital stay was determined in the previa-accreta group. In the complete PP and previa-accreta groups, the mean blood loss, the rate of admission to intensive care unit (ICU), and the rate of hysterectomy were significantly higher. The rate of preterm birth was significantly higher in the previa-accreta group than the other groups. The groups were similar with respect to mean gestational week at birth and birthweight. In the comparison of complete PP cases with the non-complete PP (low-lying, marginal and partial PP), the need for blood products transfusion, the risk of placenta accreta, peripartum hysterectomy, postpartum haemorrhage, and follow-up in the ICU were increased in the complete PP group. Discussion: The coexistence of placenta previa-accreta increases maternal-neonatal morbidity. Compared to cases with complete PP; low-lying, marginal, and partial PP do not result in an increase in maternal-neonatal morbidity.

Keywords
Placenta Previa; Placenta Accreta; Maternal Outcomes; Neonatal Outcomes

DOI: 10.4328/JCAM.4859 Received: 08.11.2016 Accepted: 01.01.2017 Printed: 01.07.2017 J Clin Anal Med 2017;8(4): 341-5
Corresponding Author: Alev Özer, Kahramanmaraş Sütçü İmam Üniversite Hastanesi, Kahramanmaraş, Türkiye.
T.: +90 3442803434 F.: +90 3443113005 E-Mail: serdarztb78@gmail.com

Introduction

Postpartum haemorrhage is responsible for more than 30% of maternal mortality and the primary cause of this is uterine atonia. However, together with the increasing rates of caesarean section (CS), particularly in recent years, placenta previa (PP) and placenta accreta (PA) have started to be recognized as leading causes of postpartum haemorrhage [1].

Placenta previa, which is defined as the placenta being located close to the internal cervical os or partially or completely covering the os, increases the risk of maternal and fetal morbidity and mortality. The maternal risks include massive bleeding, injury to adjacent organs, infection, and emergency hysterectomy [1, 2]. Prevalence of PP has been reported as 0.28%-4.8% [2-4]. Factors increasing the risk of PP include advanced maternal age, smoking, multiple pregnancies, and history of CS [4, 5].

Patients with placenta previa often present with painless bleeding at the end of the 2nd trimester or in the 3rd trimester. In addition to the maternal risk of antepartum bleeding, it can also be a reason for premature birth and consequently, for the morbidity and mortality associated with prematurity in neonates [6]. It has been reported that in cases of placenta previa, periods of hospitalisation are longer, intra-operative blood loss is increased, and especially in cases combined with accreta, there is an increased need for blood transfusion [1].

Placenta accreta is defined as the attachment of chorionic villi to the myometrium or extending beyond the myometrium to attach to the serosa and adjacent organs because of a defect in the decidua. The most significant risk factors for PA are a history of CS, placenta previa, and advanced maternal age. In patients with a history of placenta previa, as the number of CS increases, so the risk of placenta accreta increases [5, 7]. It is thought that defective endometrial repair and hypoperfusion in the scar line following CS increase the risk of PA [8].

Not separating adherent placenta from the fetus after birth can cause massive bleeding resulting in complications such as peripartum hysterectomy, disseminated intravascular coagulation (DIC), a need for blood transfusion, acute renal failure, and even maternal mortality. In cases with a history of CS, PA has been reported as the reason for performing peripartum hysterectomy, the incidence increasing from 5.4% to 46.5% [9]. Increased fetal morbidity and mortality are associated not with PA itself, but with preterm birth.

In the literature search, we found only a limited number of recent studies comparing the outcomes of pregnancies complicated by different types of placenta previa, namely low-lying previa, marginal previa, and complete previa [10-13]. To the best of our knowledge, the current study is the first to compare all subtypes of placenta previa and placenta previa/accreta with respect to demographic characteristics and maternal-neonatal outcomes.

Material and Method

This retrospective study was conducted in the Gynaecology and Obstetrics Clinic of Sütcü Imam University Hospital, which is a third stage reference hospital. Approval for the study was granted by the Local Ethics Committee.

A retrospective examination was made of the medical records of patients diagnosed with placenta previa in our clinic between January 2014 and December 2015. Data related to the demographic and clinical characteristics of the patients were obtained from these records.

In our clinic, all patients with suspected PP were routinely evaluated with transabdominal or transvaginal ultrasonography (USG) with an empty bladder. Based on previous publications about diagnosis and classification of PP, cases with a distance of <2cm between the lower edge of the placenta and the internal cervical os but in which the placenta had not reached the os, were accepted as cases of low-lying placenta [14, 15]. Reaching the internal os but not covering the os was evaluated as marginal PP, partially covering the os as partial PP, and completely covering the os as complete PP.

The diagnosis of PP was confirmed with a repeated USG evaluation one day before the CS was to be applied. In cases undergoing emergent CS, the type of PP was classified based on the last antenatal USG examination and was confirmed intra-operatively.

Gestational age was calculated according to the last menstrual period and first-trimester ultrasound. Patients with multiple pregnancy and those without adequate antenatal surveillance were excluded from the study.

In the CS procedure, the uterus lower segment incision was made 1-2cm above the placenta termination line as seen on USG. For haemostasis of bleeding in the placental bed, separated sutures together with medical treatment were used. In cases where bleeding persisted despite these steps, uterine tamponade with a Bakri balloon, uterine artery ligation, internal iliac artery ligation, or hysterectomy were applied.

All patients with a history of CS and all PP cases were evaluated with gray USG and Doppler USG in respect of placenta accreta. The absence of a sonolucent area between the myometrium and the placenta, the visualisation of lacunae with turbulent flow in the placenta, placental tissue extending beyond the uterus to the bladder or vascularisation, and thinning or loss of a hyperechoic uterine serosa – bladder interface were evaluated as PA [16].

In PA cases, after abdominal entry with a midline infra-umbilical incision, the uterus and bladder were evaluated in respect of placenta percreta. Cases with increased vascularisation in the uterine serosa and vascularisation extending over the bladder and/or adjacent tissues were evaluated as placenta percreta [16].

In PA cases, any attempt to separate the placenta manually was avoided as this can result in massive bleeding. Following a classic uterine incision and delivery of the fetus, the cord was clamped, and a hysterectomy was performed. Before closure of the abdomen, an intra-abdominal drain was inserted.

The clinical diagnosis of PA was confirmed histopathologically in all of the hysterectomised patients. Cases that were not diagnosed with PA in the antenatal period but where the placenta could not be separated following the delivery of the fetus in the CS procedure, were accepted as PA.

The blood bank was consulted and 4 units of erythrocyte suspension and 4 units of fresh frozen plasma were prepared and available preoperatively for all the cases of placenta previa and/or accreta.

Based on the ultrasonographic, intra-operative, and if present, histopathologic diagnosis, 213 placenta previa cases were recruited into 5 groups: 1-low-lying PP, 2-marginal PP, 3-partial PP, 4-complete PP and 5-PP+ accreta. The Groups 1 to 4 included the placenta previa cases without accreta. These 5 groups were compared in respect of demographic characteristics, maternal, and neonatal outcomes.

All statistical analyses were performed using the Statistical Package for Social Sciences version 18.0 (SPSS IBM Software, Armonk, NY, USA). Continuous variables were expressed as mean±SD, categorical variables as number (n) and percentage (%) and were compared using the Chi-square test. All numerical variables were normally distributed, and the mean values were compared with analysis of variance. Group comparisons were made using the post-hoc Sidak test.

The Mantel-Haenszel Chi-square test was used to determine the adjusted odds ratios (OR) with 95% confidence intervals (CI) for the complications associated with subtypes of placenta previa. A value of $p < 0.05$ was considered statistically significant.

Results

In the total 3528 live births during the study period, the incidence of placenta previa was determined as 6.0%. Of the 213 PP cases, 28.7% were lower segment previa, 10.3% marginal placenta previa, 13.1% partial placenta previa, 32.9% total previa, and 15.0% placenta previa-accreta.

The demographic characteristics of the patients are shown in Table 1. The groups were similar in respect of maternal age and gestational age at birth. The mean gravida and parity in the previa-accreta group were statistically significantly higher than in the other groups (p=0.014 and p=0.011 respectively). In 93% (197/213) of the patients there was a history of CS. The mean number of previous CS was statistically significantly higher in the previa-accreta group than in the other groups (p=0.015) (Table 1).

The groups were similar in respect of the preoperative haemoglobine (Hb) level but the postoperative Hb level was determined to be statistically significantly lower in the previa-accreta group than in the other groups (p=0.046) (Table 2).

The estimated mean blood loss was determined to be statistically significantly higher in the previa-accreta and complete previa groups compared to the other groups (p=0.01). The number of patients administered with blood products transfusion was determined to be statistically significantly higher in the previa-accreta and complete previa groups compared to the other groups (p=0.03) (Table 2).

The number of patients under Intensive Care Unit (ICU) observation in the postoperative period was determined to be higher in the previa-accreta and complete previa groups (p=0.01). The mean duration of hospitalisation was determined as statistically significantly longer in the previa-accreta group than in the other groups (p=0.013) (Table 2).

Hysterectomy was applied to 34 (16%) placenta previa cases. Of these, 26 hysterectomies were performed due to placenta accreta and the other 8 were due to persistent bleeding in the placental bed in previa cases without placenta accreta. The rate of patients to whom hysterectomy was applied was statistically significantly higher in the previa-accreta and complete previa groups (p=0.01) (Table 2).

In Group 5 (coexistence of previa+accreta), a significantly higher rate of peripartum hysterectomy, of blood product transfusion, and of stay in ICU, and a higher amount of blood loss were determined compared to Group 4 (complete previa without accreta) (Table 2).

Bladder repair was applied to a total of 7 placenta previa cases, 6 of which were previa-accreta and one of which was complete placenta previa. In 6 cases with previa-accreta, the bladder dome could not be disssected from the uterus lower segment; because of active bleeding, the upper 1/4-1/5 segment of the bladder was excised and primary repair was applied to the remaining bladder tissue. A Foley catheter was inserted in the patients who underwent bladder repair and was removed after 14 days.

The neonatal results are shown in Table 3. Although the lowest mean gestational age at birth was found in the previa-accreta group, there was no statistically significant difference between the groups (p=0.113). The rate of preterm birth (<37 completed weeks) was statistically significantly higher in the previa-accreta group than the other groups (p=0.023). The groups were found to be similar in respect of birthweight and the 1st and 5th minute Apgar scores (p=0.325, p=0.638, p=0.292). No statistically significant difference was determined between the groups with respect to the rate of neonates with a birthweight <2500 gr (p=0.524).

In 31.2% of the placenta previa cases, the diagnosis of placenta accreta was made intra-operatively and in 68.8% of the cases, placenta accreta was diagnosed in the antenatal USG examination. In 12 cases diagnosed with accreta on antenatal USG, accreta was not determined intra-operatively.

No maternal or neonatal mortality occurred in any case.

In the analysis of pregnancy and neonatal outcomes in the complete type of placenta previa (including 70 cases with complete PP alone and 27 cases with complete PP+placenta accreta, n=97) and the non-complete type (including 62 cases with low-lying, 22 cases with marginal, 27 cases with partial PP alone, and 5 cases with partial PP+placenta accreta, n=116), adjustment was made for the placenta accreta as the possible confounding factor. The complete placenta previa was determined to increase the risk of the development of accreta (OR=8.8, 95% CI=4.2-13.4, p=0.001), a prolonged hospital stay (OR=5.0, 95% CI=2.3-10.8, p<0.001), a requirement for ICU follow-up (OR=4.9, 95% CI=2.4-29.6, p<0.001, postpartum bleeding (OR=17.5, 95% CI=4.9-60.9, p<0.001), a need for transfusion of blood products (OR=3.3, 95% CI=1.8-6.0, p<0.001), and hysterectomy (OR=28.3,

Table 1. Demographic characteristics of the patients

	Low-lying previa (n= 62)	Marginal previa (n=22)	Partial previa (n=27)	Complete previa (n=70)	Previa-accreta (n=32)	P value
Age *	31.1±4.6	30.8±3.9	32.6±4.1	31.4±2.7	34.1±5.3	0.126
Gravida*	3.29±0.4	3.2±1.0	3.3±0.7	3.8±1.1	4.9±0.4	0.014† ‡
Parity*	1.6±0.2	1.7±0.7	1.9±1.0	2.2±0.9	2.9±0.5	0.011† ‡
Number of previous CS*	1.3±0.5	1.4±0.2	1.4±0.3	1.8±0.8	2.3±1.2	0.015† ‡

* Values are given as mean ± standart deviation
†p<0.05 was accepted to be statistically significant.
‡ Placenta previa-accreta group versus lower segment previa group, marginal previa group, partial previa group and complete previa group.
CS: Caeserean section

Table 2. Comparison of the maternal outcomes

	Low-lying previa (n=62)	Marginal previa (n=22)	Partial previa (n=28)	Complete previa (n=70)	Previa-accreta (n=32)	P value
Pre-operative Hb level (g/dL)*	11.7±1.5	11.6±2.0	11.6±1.8	11.4±2.3	11.2±2.2	0.571
Post-operative Hb (g/dL)*	10.9±0.6	11.2±1.4	11.2±1.9	10.5±0.9	9.7±1.3	0.046 ‡§
Hospital stay (days)*	3.6±0.5	3.0±0.8	3.7±1.4	4.8±1.8	7.6±2.1	0.013 ‡ §
ICU stay †	3.2	0	7.1	15.7	53.0	0.01 ‡ §II
Peripartum hysterectomy†	1.6	0	0	11.4	81.3	0.01‡ §II
Bladder injury†	0	0	0	1.4	18.8	0.229
Blood loss (mL) †	711±90	690±102	862±96	1344.2±186	2176±275	0.01 ‡§ II
Transfusion of blood products†	3.5	10.9	8.9	35.7	96.0	0.03‡§II

Hb: Haemoglobine
*Values are given as mean ± standart deviation
† Values are in percentage
‡p<0.05 was accepted to be statistically significant.
§Placenta previa-accreta group versus low-lying previa group, marginal previa group, partial previa group and complete previa group.
II Complete group versus low-lying previa group, partial previa group and marginal previa group

Table 3. Comparison of the Neonatal Results

	Low-lying previa (n= 62)	Marginal previa (n=22)	Partial previa (n=27)	Complete previa (n=70)	Previa-accreta (n=32)	P value
Birthweight (g)*	2924.1±90	2860.91	2818.39	2684.83	2605.08	0.325
Birthweight less than 2500 g*	17.6 %	18.2 %	21.4 %	27.1 %	32.0 %	0.524
1-min Apgar*	7.66	7.73	7.32	7.30	7.48	0.638
5-min Apgar*	9.03	8.86	8.43	8.59	8.72	0.292
Gestational week at birth*	36.50	37.22	36.06	35.91	34.60	0.113
Rate of pre-term births (<37 weeks) †	33.8 %	18.2 %	42.9 %	38.6 %	64.0 %	0.023‡§

*Values are given as mean ± standart deviation
†Values are in percentage
‡p<0.05 was accepted to be statistically significant.
§Placenta previa-accreta group versus low-lying previa group, marginal previa group, partial previa group and complete previa group.

95% CI=4.3-185.3, p<0.001). With respect to the rates of neonates born at full-term with a birthweight <2500 gr, of the preterm birth and Apgar score at 1 and 5 min less than 7, there was no increased risk in cases of complete PP compared to the other PP cases (Table 4).

Discussion

In this study, the incidence of PP was determined as 6.0% (213/3528). Rosenberg et al. [2] determined a rate of PP at 0.42% in a retrospective study of 771 cases of placenta previa. The higher rate in the current study can be attributed to the recruitment of low-lying placenta previa cases and to the referral of previa cases from neighborhood hospitals, because our clinic is a 3rd stage reference center.

An older maternal age and a history of CS are known risk factors for placenta previa [3, 4]. In the current study, 93% of the PP cases had a history of CS. In a previous study that examined 502 term PP cases, the rate of history of CS was determined as 27.3% [17]. The majority of PP cases with previous CS are nowadays referred by obstetricians working in 2nd stage hospitals to tertiary centers like ours for pregnancy surveillance and birth because of the possibility of placenta accreta detection during caesarean section surgery. This could explain the extremely high rate of history of CS in the current study.

In a prospective study that analysed 3,841 births, PA incidence was determined as 26.9% in 52 cases of major placenta previa (complete previa+partial previa) [18]. This rate was 12.7% in the current study, which can be explained by the inclusion of cases of marginal and lower segment previa in addition to major placenta previa. In the same previous study, bladder injury was reported as 13.2% and hysterectomy as 15.1%. Similarly, the rate of hysterectomy in the current study was 16%.

In a retrospective study of 64,359 births, placenta accreta prevalence was reported as 1/533. Of the PA cases in that study, 50% had a history of CS and 31.5% had placenta previa [19]. The scope of the current study was not all PA cases, but only cases of PA together with placenta previa. Therefore it was not possible to calculate the PA incidence within all births. All the previa-accreta cases in the current study had a history of CS. The mean number of previous CS in the previa-accreta group was significantly higher than in the other groups. Although not statistically significant, the maternal age of the previa-accreta group was determined to be higher than that of the other groups; this can be attributed to the higher number of gravida in that group.

Similar to the findings of the current study, Usta et al. [13] have reported a significantly increased amount of intra-operative bleeding and prolonged hospitalisation period in previa-accreta cases. The rates of blood transfusion and caesarean hysterectomy were found to be 21.9% and 5.3%, respectively, in a retrospective study involving 771 PP cases [2]. Those rates were higher in the current study. This discrepancy could be explained by the higher rate of accreta cases in the current study compared to that study (12.7% vs 3.0%). The risk of peripartum hysterectomy was determined to be increased by presence of complete placenta previa alone without accreta and by coexistence of placenta previa+accreta in the current study.

Previous studies have reported that in addition to maternal complications, placenta previa carries an increased risk of premature birth, low birthweight (<2500gr) in term births, and neonatal mortality [2, 13]. In contrast, Crane et al. [6] have reported that placenta previa was not associated with a restricted fetal growth. In the current study, though statistically insignificant, the mean neonatal weight was determined to be lower in the previa-accreta and complete previa groups than in the other groups. In accordance with the results of a review and meta-analysis by Vahanian et al. [20], the currrent study elucidated that the presence of placenta previa-accreta increased the risk of preterm birth.

Table 4. Analysis of maternal and neonatal outcomes in placenta previa

	Complete Previa (n= 97)*	Non-complete previa (low-lying, marginal, partial) (n=116)*	Odds ratios adjusted for placenta accreta (%95 CI)
Hysterectomy			28.3 (4.3-185.3) †
Applied	35.1	0	
Not applied	64.9	100.0	
Pospartum bleeding (> 1500 ml)			
Yes	79.1	4.8	17.5 (4.9-60.9) †
No	20.9	95.2	
Follow-up in ICU			
Yes	84.3	5.6	4.9 (1.5-16.2) †
No	15.7	94.4	
Blood products transfusion			
Yes	64.9	11.9	3.3 (1.8-6.0) †
No	35.1	88.1	
Hospital stay			
>2 days**	87.1	24.0	5.0 (2.3-10.8) †
≤ 2 days	12.9	76.0	
Accreta			
Yes	27.8	4.3	8,8(4,2-13,4) †
No	72.2	95.7	
Gestational age at birth (weeks)			
≥37	61.4	66.4	-
<37	38.6	33.6	
1-minute Apgar			
≥7	51.4	44.7	-
<7	48.6	55.3	
5-minute Apgar			
≥7	72.1	61.5	-
<7	27.9	38.5	
Birthweight			
≥2500 g	28.8	23.5	-
<2500g	71.2	76.5	

Data were presented as Mantel-Haenszel adjusted Odds ratio
*Values are in percentage
CI: Confidence interval
† p <0.001

Satija [21] reported USG to have 87.5% sensitivity and 86.4% specificity for placenta accreta. In the current study, USG sensitivity and specificity for placenta accreta were determined as 68.8% and 93.8%, respectively.

Conclusion
To best of our knowledge, this was the first study to analyse the association of maternal and neonatal outcomes with different types of placenta previa and with previa-accreta. The combination of placenta previa + accreta increases maternal morbidity compared to PP cases without accreta. Compared to cases with complete PP, low-lying, marginal, and partial PP do not result in an increase in maternal and neonatal morbidity.

Competing interests
The authors declare that they have no competing interests.

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How to cite this article:
Özer A, Sakallı H, Köstü B, Aydoğdu Ş. Analysis of Maternal and Neonatal Outcomes in Different Types of Placenta Previa and in Previa-accreta Coexistence. J Clin Anal Med 2017;8(4): 341-5.